General

Guideline Title

Recommendations for optimal warfarin management for prevention of thromboembolic events in patients with atrial fibrillation.

Bibliographic Source(s)

Canadian Agency for Drugs and Technologies in Health (CADTH). Recommendations for optimal warfarin management for prevention of thromboembolic events in patients with atrial fibrillation. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2011 Nov. 20 p. [13 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Question 1: What is the role of specialized anticoagulation services or other anticoagulation management options for the optimal management of warfarin therapy?

Recommendation: The Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) Expert Review Committee (CERC) recommends that patients with non-valvular atrial fibrillation (NVAF) requiring warfarin be managed by a well-coordinated, structured approach dedicated to their anticoagulation therapy.*

*This does not need to be restricted to specialized anticoagulation clinics.

Values and Preferences

During their deliberations, committee members identified the following considerations as important (in no order of preference):

- Rate of adoption of warfarin therapy can be limited based on patient beliefs (e.g., stigma associated with "rat poison") and preferences.
- The need for decision aids that outline the frequency and severity of strokes versus bleeds with warfarin therapy for atrial fibrillation (AF), to be more broadly used in practice to enable patients to consider their own preferences regarding the relative importance of preventing stroke and risking bleeds.
- Patient convenience and the impact on burden of treatment (e.g., need for laboratory services or clinic visits).
- Personal costs to patient.
- Maintenance of continuity of care. Patients on warfarin often have multiple other medical conditions that must be addressed along with AF.
- Ability to reach therapeutic range quickly and efficiently.

- Role of anticoagulation clinics early versus later in therapy should be considered (e.g., effect on international normalized ratio [INR] and impact on thrombosis and bleeding risk at treatment initiation).
- Need to define coordinated care (e.g., communication between care providers regarding warfarin treatment pre- and post-surgery)
- Equity issues versus patient choice and/or preference.
- Use of warfarin is associated with many barriers (some are serious, preventing some patients from electing to use warfarin).

Question 2: What is the role of patient self-testing (PST) and patient self-management (PSM) for the optimal management of warfarin therapy?

Recommendation: CERC does not recommend self-management for most patients with NVAF requiring warfarin.

Values and Preferences

During their deliberations, committee members identified the following considerations as important (in no order of preference):

- There may be a niche for PST or PSM as part of a well-coordinated and structured approach to anticoagulation therapy with some patients (e.g., remote areas).
- There is a need to provide a choice between organized care and PST or PSM to patients.
- Carefully selected patients may be considered for PST or PSM. Access issues could make the costs acceptable.

Question 3: In remote areas, what types of anticoagulation management options can be recommended?

Statement: CERC determined that there is no evidence to make a recommendation on the role of warfarin management options in remote areas.

Values and Preferences

During their deliberations, committee members identified the following considerations as important (in no order of preference):

- There is no evidence available to support a recommendation on this question.
- Access to warfarin management services may be limited due to cost associated with distance in remote areas.
- Remote areas are an example where PST testing may be considered.
- There may be a niche for PST or PSM as part of a well-coordinated and structured approach to anticoagulation therapy with some patients (e.g., remote areas).
- Carefully selected patients may be considered for PST or PSM. Access issues could make the costs acceptable.
- The lack of evidence regarding warfarin management options in remote areas is a major research gap.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Thromboembolic events associated with non-valvular atrial fibrillation

Guideline Category

Management

Prevention

Treatment

Clinical Specialty

Cardiology

Family Practice

Geriatrics

Hematology

Internal Medicine

Pharmacology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Utilization Management

Guideline Objective(s)

- To provide recommendations for the optimal management of warfarin for the prevention of thromboembolic events in patients with atrial fibrillation
- To help health care decision-makers, patients, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services

Target Population

Patients with non-valvular atrial fibrillation requiring warfarin therapy

Interventions and Practices Considered

1. Use of specialized anticoagulation services versus other options for the optimal management of warfarin therapy
2. Patient self-testing and patient self-management of warfarin therapy (not recommended routinely)
3. Role of warfarin management options in remote areas (no recommendation made)

Major Outcomes Considered

- Time in therapeutic international normalized ratio (INR) range
- Stroke (ischemic, hemorrhagic, transient ischemic attack, any)
- Systemic embolism
- Bleeding (major, minor, fatal, intracranial, gastrointestinal)
- Quality of life
- Mortality
- Costs
- Resource utilization
- Incremental cost-effectiveness ratio

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

The evidence for developing recommendations on the optimal management of warfarin for preventing thromboembolic events in patients with atrial fibrillation was derived from Canadian Agency for Drugs and Technologies in Health (CADTH) science reports. The Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) Expert Review Committee (CERC) members had access to the bibliographies of these reports early in the process (see the "Availability of Companion Documents" field).

Systematic Review

Research Questions

1. What are the clinical benefits and harms associated with the use of individual specialized anticoagulation services, compared with usual care for adult patients receiving long-term warfarin therapy?
2. What are the clinical benefits and harms associated with the use of one type of specialized anticoagulation service compared with another type, for adult patients receiving long-term warfarin therapy?
3. What are the costs associated with specialized anticoagulation services?

Literature Search Strategy

The literature search was performed by an information specialist using a peer-reviewed search strategy. Published literature was identified by searching the following bibliographic databases: MEDLINE (1946 to present) with in-process records and daily updates via Ovid; EMBASE (1980 to present) via Ovid; The Cochrane Library (2011, Issue 5) via Wiley; and PubMed. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were warfarin and specialized anticoagulation services. Keywords were searched in title only and controlled vocabulary restricted to major subject headings.

Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and non-randomized studies. Conference abstracts were excluded from the search results. Where possible, retrieval was limited to the human population. Retrieval was also limited to documents published between January 1, 2006, and May 31, 2011. The initial search was completed on May 31, 2011. Regular alerts were established to update the search until the publication of the final report.

Additionally, a search on warfarin and atrial fibrillation was conducted using the same databases listed above. Methodological filters were applied

to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and guidelines. Retrieval was also limited to documents published between January 1, 2006, and May 12, 2011. The initial search was completed on May 12, 2011. Regular alerts were established to update the search until the publication of the final report.

Grey literature (literature that is not commercially published) was identified by searching the health technology assessment agencies and guidelines sections of the Grey Matters checklist (www.cadth.ca/resources/grey-matters). Google and other Internet search engines were used to search for additional web-based materials. These searches were supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry.

The authors of this report also consulted the primary authors of the 2012 American College of Chest Physicians guidelines on management of anticoagulation therapy.

Selection Criteria and Method

Two reviewers independently screened citations and selected health technology assessments (HTAs), systematic reviews, meta-analyses, randomized controlled trials, and non-randomized studies regarding specialized anticoagulation services for management of warfarin dosing. The decision to order an article was based on the title and abstract, where available. In cases of insufficient information, the article was ordered. The same two reviewers selected the final articles for inclusion based on full-text publications. An article was included for review according to selection criteria established a priori (see below). Any disagreement between reviewers was discussed until consensus was reached.

Selection criteria were defined for population, intervention, comparator, outcomes, and study designs (see section 5.2 in the systematic review; see the "Availability of Companion Documents" field).

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria; focused only on patients with mechanical heart valves; were narrative reviews or editorials; were performed in a pediatric population; or were included in a selected HTA, systematic review, or meta-analysis. Additionally, systematic reviews were excluded if all reviewed studies were included in a more recent systematic review or meta-analysis.

Number of Source Documents

Twenty-seven publications were included in the clinical systematic review from the electronic literature search, search of grey literature, and hand searching. Of these, nine were health technology assessments or systematic reviews, and 18 were primary studies (6 randomized controlled trials and 12 non-randomized controlled trials).

Four articles were identified for inclusion in the economic report from the limited literature search, including one cost-utility study and three costs analyses.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The evidence for developing recommendations on the optimal management of warfarin for preventing thromboembolic events in patients with atrial

fibrillation was derived from the Canadian Agency for Drugs and Technologies in Health (CADTH) science reports. The Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) Expert Review Committee (CERC) members had access to the bibliographies of these reports early in the process (see the "Availability of Companion Documents" field).

Data Extraction Strategy

One reviewer extracted clinical and economic data for each article to tabulate relevant characteristics and outcomes from the included studies. Data extraction was verified by a second reviewer to confirm accuracy.

Critical Appraisal of Individual Studies

Two reviewers independently appraised the included studies. The quality of systematic reviews was evaluated using the AMSTAR instrument. The quality of randomized controlled trials and non-randomized studies was assessed using the Downs and Black instrument. Methodological quality of clinical effectiveness evidence was evaluated based on randomization, adequate concealment of randomization, degree of blinding, use of intention to treat analysis, and description of dropouts and withdrawals, where appropriate. A numeric score was not calculated for each study; instead, strengths and limitations were described. Any disagreements were resolved through discussion until consensus was reached.

The BMJ checklist was used to evaluate the quality of the cost-utility study. The key limitations were described for the other study types. Study results were described using a narrative approach.

Data Analysis Methods

Because of heterogeneity present across the selected studies, a formal meta-analysis was not conducted. Studies were described using a narrative approach.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Project Overview

Once a topic is selected, the Canadian Agency for Drugs and Technologies in Health (CADTH) undertakes activities related to key areas in the procedure. The Optimal Use Working Group and the Formulary Working Group will provide advice and guidance throughout the process, through to supporting intervention and evaluation tools. The Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) Expert Review Committee (CERC) provides expert advice and recommendations on the topic area relating to the identification, evaluation, and promotion of optimal prescribing and use of drugs. A broad range of stakeholders are invited to provide feedback at key stages in the CADTH process.

Three specific questions were asked to CERC members:

- Question 1: What is the role of specialized anticoagulation services or other anticoagulation management options for the optimal management of warfarin therapy?
- Question 2: What is the role of patient self-testing and patient self-management for the optimal management of warfarin therapy?
- Question 3: In remote areas, what types of anticoagulation management options can be recommended?

COMPUS Expert Review Committee Process and Perspective

CERC members consider clinical effectiveness (i.e., benefits and harms), burdens, and cost data when formulating Optimal Use Recommendations. Committee members bring their individual expertise and experience to bear (as experts, general practitioners, interventionists, consumers, and members of the public) and draw upon their own values and preferences to discuss the evidence and reach conclusions.

Detailed information regarding the recommendations (i.e., vote results, the rating of overall quality of clinical evidence, underlying values and preferences related to the recommendations and notes from CERC deliberations) is provided in Appendix B and Appendix C of the original guideline document.

CERC Voting Process

During their deliberations, CERC members were asked to make recommendations for each question, based on clinical evidence, economic evidence, and values and preferences. CERC members were also asked to rate the quality of evidence for each question. Recommendations were first formulated based on consideration of the clinical evidence, followed by a round of voting. Recommendations were then revised based on economic evidence and values and preferences, followed by a final round of voting.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The objective was to review the published literature for Canadian studies that provided information on the following question: What are the costs associated with specialized anticoagulation services? See the Economic Evidence Report for full details of the methodology and results of the Review of Canadian Economic Studies (see the "Availability of Companion Documents" field).

Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) Expert Review Committee (CERC) Consideration of Economic Evidence

Question 1: What is the role of specialized anticoagulation services or other anticoagulation management options for the optimal management of warfarin therapy?

The committee considered the results of a review of published literature containing information on Canadian costs associated with specialized anticoagulation services. Three costing studies provided information on the costs of different models of specialized anticoagulation services and usual care in Canadian settings.

Key findings suggest that the literature evaluating the relative costs of hospital-based services (either managed by physicians or pharmacists) compared with community physician-managed care was inconclusive. Anticoagulation services were associated with lower costs in two studies, and higher costs in a third. Not all relevant costs were considered in these studies.

Question 2: What is the role of patient self-testing (PST) and patient self-management (PSM) for the optimal management of warfarin therapy?

The committee considered the results of a review of published literature containing information on Canadian costs associated with PST or PSM. One cost-utility analysis provided information on PSM versus physician-managed anticoagulation from a Canadian health payer perspective.

Key findings suggest the following:

- The incremental cost-effectiveness ratio of PSM compared with physician management of anticoagulation was Canadian (C) $14,000 over a five-year period.
- Costs for PSM were high in the first year due to start-up costs of C$1,567 per patient for training and support.
- Mean incremental costs were C$1,420 more for PSM versus usual care for the first year, C$989 per year after five years, and C$599 per year after 10 years. These are aggregate costs. Costs in the PSM strategy were partially offset by a reduction in costs associated with clinical events (hemorrhage, thromboembolic event) compared with physician management.

Question 3: In remote areas, what types of anticoagulation management options can be recommended?

No economic evidence was available regarding the costs associated with different warfarin management options in remote areas.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

A broad range of stakeholders are invited to provide feedback at key stages in the Canadian Agency for Drugs and Technologies in Health (CADTH) process.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The recommendations are based on clinical evidence (health technology assessments, systematic reviews, randomized controlled trials and non-randomized trials), economic evidence, and values and preferences.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Optimal warfarin management for prevention of stroke, systemic embolism, and bleeding events in patients with atrial fibrillation

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

- The information in this report is intended to help health care decision-makers, patients, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. The information in this report should not be used as a substitute for the application of clinical judgment in respect to the care of a particular patient or other professional judgment in any decision-making process, nor is it intended to replace professional medical advice. While the Canadian Agency for Drugs and Technologies in Health (CADTH) has taken care in the preparation of this report to ensure that its contents are accurate, complete, and up-to-date, CADTH does not make any guarantee to that effect. CADTH is not responsible for any errors or omissions or injury, loss, or damage arising from or as a result of the use (or misuse) of any information contained in or implied by the information in this report.
- CADTH takes sole responsibility for the final form and content of this report. The statements, conclusions, and views expressed herein do not necessarily represent the view of Health Canada or any provincial or territorial government.

Implementation of the Guideline

Description of Implementation Strategy

The Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) Expert Review Committee (CERC) Process and Perspective

CERC develops recommendations and advice to contribute to optimal health outcomes and to foster a sustainable health care system for Canadians. CERC considers the practical needs of policy-makers, health care providers, and consumers in implementing and using the recommendations and advice toward the promotion of optimal practices. To assist with the interpretation of the recommendations and provide commentary relating to the evidence, key statements from CERC deliberations are noted in the original guideline document.

Next Steps

The Optimal Use Recommendations will be widely disseminated to encourage uptake and implementation by decision-makers at various levels (e.g., policy decision-makers, health care professionals, and patients). Gaps in practice and knowledge related to the use of warfarin will be identified by comparing the final recommendations with information on current practice and utilization of these products in Canada.

Key messages to promote the optimal warfarin management for the prevention of thromboembolic events in patients with atrial fibrillation will be developed to address identified gaps in practice and knowledge. Intervention tools will be populated with the key messages and related evidence for implementation across Canada.

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Canadian Agency for Drugs and Technologies in Health (CADTH). Recommendations for optimal warfarin management for prevention of thromboembolic events in patients with atrial fibrillation. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2011 Nov. 20 p. [13 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Nov

Guideline Developer(s)

Canadian Agency for Drugs and Technologies in Health - Nonprofit Organization

Source(s) of Funding

Production of this report is made possible through a financial contribution from Health Canada.

Guideline Committee

Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) Expert Review Committee (CERC)

Composition of Group That Authored the Guideline

Participating Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) Expert Review Committee (CERC) Members: Dr. Lisa Dolovich (*Chair*), Research Director and Associate Professor, Department of Family Medicine, McMaster University Ambulatory Care Pharmacotherapy Specialist, St. Joseph's Healthcare Hamilton, Associate Director, Centre for Evaluation of Medicines; Dr. Michael Allen, Associate Professor, Director, Evidence-based Programs, Continuing Medical Education, Dalhousie University; Dr. Michael Evans, Director, Patient Self-Management and Knowledge Support, Centre for Effective Practice, Department of Family and Community Medicine, University of Toronto; Dr. Scott Klarenbach, Associate Professor, Department of Medicine, Division of Nephrology, University of Alberta, Fellow, Institute of Health Economics; Ms. Cathy MacNutt, Public Member; Panos Petrides, Public Member; Dr. Jim Silvius, Senior Medical Director, Seniors' Health, Alberta Health Services, Associate Professor, Division of Geriatric Medicine, Department of Medicine, University of Calgary; Dr. Adil Virani, Director, Pharmacy Services, Fraser Health Authority, Associate Professor, Faculty of Pharmaceutical Sciences, University of British Columbia

Specialist Members: Dr. Marc Carrier, Associate Scientist, Clinical Epidemiology, Ottawa Hospital Research Institute, Physician, Hematology (Thrombosis), The Ottawa Hospital, Assistant Professor, Department of Medicine, University of Ottawa; Dr. Agnes Y. Lee, Associate Professor of Medicine, Division of Hematology, University of British Columbia, Medical Director, Thrombosis Program, Vancouver Coastal Health, Diamond Health Care Centre; Dr. Jafna Cox, Heart and Stroke Foundation Endowed Chair in Cardiovascular Outcomes, Director of Research, Division of Cardiology, Professor, Departments of Medicine and of Community Health and Epidemiology, Dalhousie University, Staff Cardiologist, Capital Health; Dr. Anne Holbrook, Professor and Director, Division of Clinical Pharmacology and Therapeutics, Department of Medicine, McMaster University, Senior Scientist, Centre for Evaluation of Medicines, Staff Physician, St. Joseph's Healthcare Hamilton, Staff Physician, Hamilton Health Sciences; Dr. Mario Talajic, Cardiac electrophysiologist, Director, Cardiac Genetics Centre, Montreal Heart Institute, JC Edwards Professor of Medicine, Director, Specialty Training Programs, Department of Medicine, University of Montreal; Dr. Leslie Zypchen — designated backup for Dr. Agnes Lee (sharing votes), Clinical Assistant Professor, Division of Hematology, University of British Columbia, Staff Hematologist, Vancouver General Hospital

Contributors from Canadian Agency for Drugs and Technologies in Health (CADTH): Mr. Chris Kamel, Clinical Research Officer; Ms. Gaetanne Murphy, Clinical Research Officer; Ms. Agnieszka Kus, Clinical Research Assistant; Ms. Kelly Farrah, Information Specialist; Ms. Heidi Staples, Clinical Research Officer; Dr. Janice Mann, Knowledge Exchange Officer; Ms. Kasia Kaluzny, Knowledge Exchange Officer; Ms. Andra Morrison, Environmental Scanning Officer; Dr. Mohammed Jabr, Health Economist; Dr. Vijay Shukla, Senior Advisor, Advancing the Science; Mr. Michel Boucher, Theme Lead, Cardiovascular and Cerebrovascular; Dr. Srabani Banerjee, Manager, Clinical Research; Dr. Chander Sehgal, Director, Formulary Reviews, Acting Director, Optimal Use and Health Technology Assessment; Mr. Denis Belanger, Director, Impact, Partnership and Outreach

Financial Disclosures/Conflicts of Interest

No members declared any conflicts of interest. Conflict of Interest Guidelines are posted on the Canadian Agency for Drugs and Technologies in Health (CADTH) Web site .

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Canadian Agency for Drugs and Technologies in Health (CADTH) Web site .

Availability of Companion Documents

The following are available:

- Optimal warfarin management for the prevention of thromboembolic events in patients with atrial fibrillation: a systematic review of the clinical evidence. Ottawa (ON): Canadian Agency for Drugs and Technology in Health (CADTH); 2011 Nov. 44 p. Electronic copies: Available in Portable Document Format (PDF) from the Canadian Agency for Drugs and Technology in Health (CADTH) Web site .
- Optimal warfarin management for the prevention of thromboembolic events in patients with atrial fibrillation: review of Canadian economic studies. Ottawa (ON): Canadian Agency for Drugs and Technology in Health (CADTH); 2011 Nov. 27 p. Electronic copies: Available in PDF from the CADTH Web site .
- Optimal warfarin management for the prevention of thromboembolic events in patients with atrial fibrillation: warfarin management in patients with atrial fibrillation — current practice study. Ottawa (ON): Canadian Agency for Drugs and Technology in Health (CADTH); 2012 Mar. 87 p. Electronic copies: Available in PDF from the CADTH Web site .
- Optimal warfarin management for the prevention of thromboembolic events in patients with atrial fibrillation: optimal use project in brief. Ottawa (ON): Canadian Agency for Drugs and Technology in Health (CADTH); 2011 Dec. 1 p. Electronic copies: Available in PDF from the CADTH Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on January 16, 2013. The information was verified by the guideline developer on March 6, 2013.

Copyright Statement

Disclaimer

NGC Disclaimer